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Exploring the Potential of NRX-101 for Pediatric Bipolar Depression: A Call for Research and Equity

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Despite longstanding recognition of the need for pediatric-specific data, many psychiatric medications prescribed to children and adolescents initially were studied primarily in adults, and for some conditions, pediatric evidence remains limited. While certain treatments are supported by robust pediatric trials; such as stimulant medications for attention-deficit/hyperactivity disorder (ADHD) (Multimodal Treatment of ADHD Study), fluoxetine for adolescent depression (Treatment for Adolescents with Depression Study), and sertraline for youth anxiety disorders (Child/Adolescent Anxiety Multimodal Study); significant gaps remain for other medications.[1-3] As a result, adolescents with severe psychiatric illness sometimes are treated with therapies whose safety and efficacy in this population are not fully established. Our patients deserve interventions grounded in rigorous pediatric research.

Emerging data on NRX-101, a fixed-dose combination of D-cycloserine (an NMDA receptor modulator) and lurasidone (an atypical antipsychotic), have generated interest for the treatment of severe bipolar depression and suicidality in adults.[4] Lurasidone already is FDA-approved for bipolar depression in youth aged 10 years and older, with demonstrated efficacy and generally favorable tolerability.[5] D-cycloserine introduces a novel mechanism by modulating NMDA receptors, which may enhance antidepressant effects while also addressing suicidality and executive functioning deficits commonly observed in adolescent bipolar disorder (e.g., impairments in attention and working memory).[6,7]

Preliminary Phase 2 trials of NRX-101 in adults suggest potential benefits for depressive symptoms and suicidality; however, detailed results have not yet been fully reported.[4] Given the substantial clinical burden and elevated risk of suicidal ideation and attempts among adolescents with bipolar disorder, further investigation in youth populations is warranted.[6]

Once adult efficacy and safety are established, academic-led, multisite randomized controlled trials will be important to evaluate NRX-101 in adolescents with treatment-resistant bipolar depression. Such studies should incorporate developmentally appropriate assessments and

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interventions and ensure equitable inclusion of youth from diverse racial, ethnic, and socioeconomic backgrounds.

It is also important to recognize that trial outcomes may differ by sponsorship. Industry-sponsored studies often enroll participants with less severe symptoms, which can influence placebo response and limit generalizability, whereas academic-led trials may better reflect real-world clinical populations. Accordingly, rigorously designed academic studies are important for establishing evidence-based prescribing practices in pediatric psychiatry.

Through careful, well-designed research, the field can ensure that emerging pharmacologic innovations such as NRX-101 are both safe and effective for adolescents. Expanding pediatric trials with attention to developmental and equity considerations will strengthen the evidence base and ultimately improve psychiatric care for youth.

ARTICLE INFORMATION

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